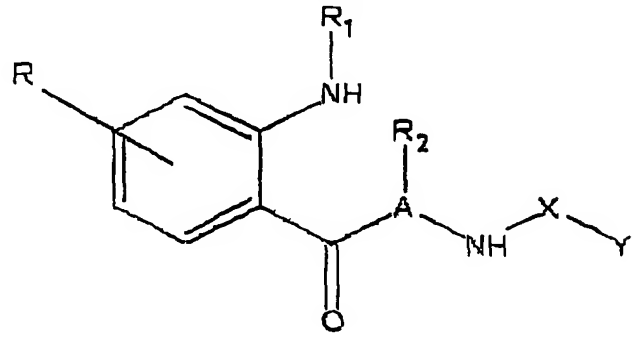
AMENDED CLAIMS

[received by the International Bureau on 18th February 2005 (18.02.05)]

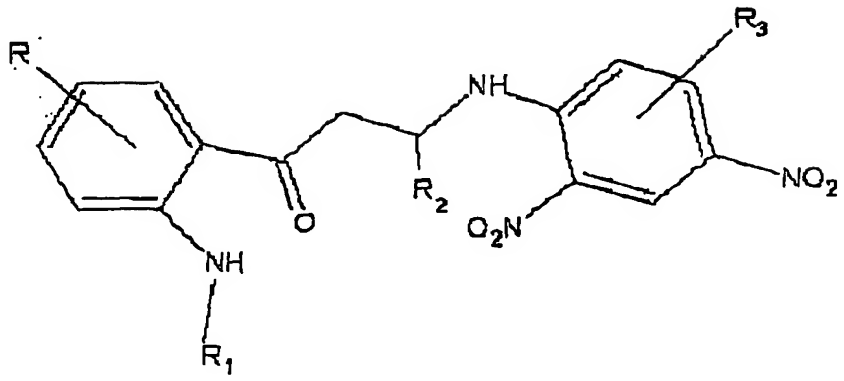
1. A compound having the formula (I):



(I)

and stereoisomers and pharmaceutically acceptable salts thereof, wherein: A is C_{1-6} alkylene; R, R_1 and R_2 are independently hydrogen, halo, haloalkyl, aryl, a heterocyclic group, a heteroaryl group, alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, hydroxyalkyl, nitro, amino, cyano, cyanamido, guanidine, amidino, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, carbonylamido, S-alkyl or alkylyhiol; X is $>C_{1-6}$ alkylene, >C=O or >C=S or a single bond; and Y is hydrogen, halo, haloalkyl, aryl, a heterocyclic group, a heteroaryl group, alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, hydroxyalkyl, nitro, amino, cyano, cyanamido, guanidine, amidino, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, carbonylamido, styryl which may be ring-substituted by up to four substituents independently selected from among hydrogen, halo, haloalkyl, aryl, a heterocyclic group, a heteroaryl group, alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, hydroxyalkyl, nitro, amino, cyano, cyanamido, guanidine, amidino, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, S-alkyl, alkylyhiol or -COQ, where Q is hydroxy, C_{1-6} alkoxy, amino, mono- C_{1-6} alkylamino, di- C_{1-6} alkylamino, hydroxylamino, C_{1-4} alkoxyamino or aryl-C_{1-4}-alkoxyamino, but excluding (a) the compounds where simultaneously X is >C=O, Y is methyl, A is CH_2CH_2, R is 5-methoxy, R_1 is H or formyl and R_2 is H, (b) the compounds where the moiety -A(R_2)-NH-X-Y is -CH_2CH(COQ)-NH_2 or –CH(haloalkyl)-CH(COQ)-NH_2, and (c) the compounds where simultaneously X is a single bond, Y is arylalkyl, A is $CH_2CH_2CH_2$, both R_1 and R_2 are H and R is 4-halo where the moiety -CO-A(R_2)-NH-X-Y is deemed to be in the 1-position of the depicted benzene ring.

2. A compound according to claim 1, having formula (II):



(II)

wherein R is hydrogen, methyl or methoxy, R_1 is hydrogen or formyl, R_2 is hydrogen or carboxyl, and R_3 is hydrogen, halo, haloalkyl, aryl, a heterocyclic group, a heteroaryl group, alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, hydroxyalkyl, nitro, amino, cyano, cyanamido, guanidine, amidino, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, carbonylamido, S-alkyl or alkylyhiol, and stereoisomers and pharmaceutically acceptable salts thereof.

3. Compounds according to claim 1, where in formula (I), Y is 2-furyl, 2-dihydrofuryl, 2-tetrahydrofuryl or (2-R°-COO-)phenyl, any of which may be substituted by 1-2 substituents selected from C_{1-4} alkyl, C_{1-4} alkoxy, OH, nitro, or Y is hydrogen or styryl which is ring-substituted by up to two substituents independently selected from among halogen, C_{1-4} alkyl, C_{1-4} alkoxy, OH, nitro, aryl, aryl-C_{1-4} alkyl, or aryl-C_{1-4} alkoxy, and stereoisomers and pharmaceutically acceptable salts thereof.

4. Compounds according to claim 1, and stereoisomers and pharmaceutically acceptable salts thereof, where in formula (I), R_2 is hydrogen and at least one of the following conditions applies, namely:

R is 5-methoxy; and/or

A is CH_2CH_2 or $CH_2CHCOOH$; and/or

R_1 is hydrogen; and/or

X is a single bond and Y is a 2,4-dinitrophenyl group.

5. Compounds according to claim 1, and stereoisomers and pharmaceutically acceptable salts thereof, where in formula (I), X and Y are selected in combination as follows:

X is -CO- and Y is 2-furyl; or

X is -CO- and Y is 2-tetrahydrofuryl; or

X is -CH_2- and Y is 2-tetrahydrofuryl; or

X is -CO- and Y is 2-acetoxyphenyl; or

X is -CO- and Y is 3,4-dihydroxystyryl or 3,4-dihydroxycinnamoyloxy.

6. Compounds according to claim 5, wherein at least one of the following conditions applies, namely:

R is 5-methoxy; and/or

A is CH_2CH_2 or $CH_2CHCOOH$; and/or

R_1 is hydrogen.

7. A compound according to claim 1, which is 3-(2-aminobenzoyl)-2-(2,4-dinitroanilino)propanoic acid, and stereoisomers and pharmaceutically acceptable salts thereof.

8. A compound according to claim 1, which is 2-(2-aminobenzoyl)-N-(2,4-dinitrophenyl)ethylamine, and pharmaceutically acceptable salts thereof.

9. A pharmaceutical formulation containing a therapeutically effective amount of at least one compound as defined in claim 1, in association with at least one pharmaceutically acceptable ingredient selected from diluents, preservatives, solubilizers, emulsifiers, adjuvants, excipients and carriers.

10. A pharmaceutical formulation according to claim 9, which is further characterized by at least one of the following features:

(i) it is adapted for oral, rectal, parenteral, transbuccal, intrapulmonary or transdermal administration;

(ii) it is in unit dosage form, each unit dosage comprising an amount of said at least one compound which lies within the range of 0.0025-1000 mg;

(iii) it is a controlled release formulation, wherein said at least one compound is released at a predetermined controlled rate;

(iv) it comprises additionally at least one known therapeutically active ingredient selected from neuroleptics, thymoleptics, anxiolitics, tranquilizers, analgesics, and antiparkinson's drugs.

11. Use of at least one compound as defined in any one of claims 1-8, or a pharmaceutical formulation as defined in claim 9 or claim 10, for the manufacture of a medicament for treatment or prevention of a physiological condition selected from stroke, ischemia, CNS trauma, hypoglycemia and surgery, CNS disorders including neurodegenerative diseases, overstimulation of the excitatory amino acids, psychiatric disorders, epilepsy and other convulsive disorders, anxiety, psychosis, senile dementia, multi-infarct dementia, chronic pain (analgesia), glaucoma, CMV retinitis, urinary incontinence, and for inducing anesthesia, enhancing cognition, and preventing opiate tolerance and withdrawal symptoms, impotence, cardiovascular disorders including hypertension, preventing blood coagulation, neuropathy, anti-inflammatory, chronobiological-related disorders, seasonal-related disorders, endocrine indications, contraception and infertility, precocious puberty, premenstrual syndrome, hyperprolactinemia, and growth hormone deficiency, neoplastic disease, other proliferative diseases (benign and tumor prostate growth), immune system disorders, conditions associated with senescence, ophthalmological diseases, cluster headache, migraine, skin-protection, diabetes stabilization and weight gain disorders, and for use in animal breeding.

STATEMENT

(A) Whereas claim 1 previously recited exclusions (a) and (b), it now excludes additionally: "(c) the compounds where simultaneously X is a single bond, Y is arylalkyl, A is $CH_2CH_2CH_2$, both R_1 and R_2 are H and R is 4-halo where the moiety -CO-A(R_2)-NH-X-Y is deemed to be in the 1-position of the depicted benzene ring."

(B) In claim 3, there was previously an error in that the symbol "X" was used instead of "Y". The obviousness of this error may be seen by comparing with the values for X and Y in claim 1. This error has now been corrected. A similar confusion between the values of X and Y in claim 4 has been addressed by amending this claim.

(C) Pages 3 and 4 of the specification have been amended to provide counterparts of the amendments made to the claims.

(D) Also, page 4 now includes a definition of "aryl" as a monovalent radical derived from an aromatic compound by removing a hydrogen atom from the aromatic nucleus. It is believed that it would be evident to the skilled addressee of this patent application, particularly with reference to specified compounds of the invention, that "aryl" must have this meaning in the present context. For external support for this definition (if necessary), reference may be made to, e.g., "Online Biology Dictionary" and "Dorland's Medical Dictionary".

We comment on the matters set forth in the Written Opinion as follows:

(1) Novelty, etc. (i) GB 1334884 (Sumitomo) – the relevant compound is excluded from the claims by clause (c) added at the end of claim 1. (ii) CAS online abstract 1972: 474963 - the specified compound requires R1=acetyl, which we do not claim.

It is submitted that all pending claims thus possess both novelty and inventive step.

(2) Clarity, etc. In view of the present amendments, it is submitted that all dependent claims clearly relate to the compounds defined in claim 1.

(3) Claim 11. This "Swiss-type" claim is in the format accepted in the EPO and other PCT members. Thus, it should be regarded as a method of treating the recited indications.